## Remarks

Upon entry of the amendments submitted herein, claims 23-82 will be pending. Claims 1-22 have been canceled previously or herein without prejudice or disclaimer. Applicants reserve the right to pursue subject matter encompassed by all canceled claims in one or more continuation or divisional applications. No new matter has been added.

## Rejection of claims 23-36, 40-53, 57-66, and 70-79 under 35 U.S.C. § 101

The rejection of claims 23-36, 40-53, 57-66, and 70-79 under 35 U.S.C. § 101 as allegedly not being supported by either a specific and substantial utility or a well established utility was maintained. See Paper No. 42005, page 2. In particular, the Examiner maintained the allegation that "the specification fails to provide sufficient objective evidence of any activity for encoded protein" and that "there is no information pertaining to the significance of the percentage homology, e.g. whether there were any conserved motifs that would lead the artisan to accept the protein's function." See Id. at 3.

Applicants respectfully disagree and traverse.

In the first Office Action mailed April 21, 2005, the Examiner introduced the currently pending utility rejection alleging that "the specification fails to provide sufficient objective evidence of any activity for encoded protein." See Paper No. 92004, page 3, last paragraph. In Applicants response to the first office action, passages from the specification were explicitly identified where an activity for the FcR-V polypeptides was indeed asserted. Specifically, Applicant's response pointed out that the specification indicates that FcR-V polypeptides are "important in the regulation of the immune and hematopoietic systems and are 'thought to function as an important trigger of complex immune defense responses'" and "are thought to play a dominant role in type II hypersensitivity reactions." See Response to first Office Action, page 13, second full paragraph. Furthermore, Applicants also identified specific immune system related disorders disclosed in the specification for which the FcR-V polypeptides would be useful in treating<sup>1</sup>.

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<sup>&</sup>lt;sup>1</sup> The specification teaches that the FcR-V polypeptides are useful for the diagnosis or treatment of specific immune system-related disorders, including "immune-complex related inflammatory diseases such as rheumatoid arthritis, systemic lupus erythmatosis, autoimmune hemolytic anemia, thromboctyopenia and IgG- or IgE-mediated inflammation, anaphylaxis, allergy ....." See, e.g., page 60, paragraph 0135.

Applicants provided explicit evidence from the specification in their previous response showing a specific biological role for the FcR-V polypeptides (i.e., regulation of the immune and hematopoietic systems) and correlated this role to a specific group of immune system-related disorders. Thus, the specific, substantial, and credible elements under 35 U.S.C. § 101 were met in that such a correlation between the biological activity and the asserted use in specific disease conditions would be, more likely than not, sufficient to convince one of skill in the art of the usefulness of the FcR-V protein. Therefore, Applicants have provided evidence of a specific, substantial, and credible utility and have clearly met their burden in rebutting the *prima facie* assertion of lack of utility. *See*, M.P.E.P. 2107 (II)(3)(i).

The Examiner also alleged in the first office action response that "there is no information pertaining to the significance of the percentage of homology, e.g. whether there were any conserved motifs that would [have] led the artisan to accept the protein's function." See, Paper No. 92004, page 4. In response, Applicants pointed to specific locations in the specification that disclosed and discussed the importance of the conserved domains between FcR-V and the Fc- $\gamma$ 2 receptor, as well as shared conserved domains between the well-established family of FcR receptors. See, Response to first Office Action, page 14, first full paragraph. See also, specification pages 4 and 5, paragraph 0012; page 19, paragraphs 0038-0039; and Figure 14.

Additionally, Applicants pointed to the reference by Raghavan et al., cited in the specification, which discloses that "receptors for the Fc domain of immunoglobulins play an important role in immune defense" and the "biological responses elicited [by Fc receptors] antibody-dependent, cell-mediated cytotoxicity, release of include phagocytosis, inflammatory mediators, and regulation of lymphocyte proliferation and differentiation. See Id. at page 19, paragraph 0039. See also, Raghavan et al., abstract (previously submitted as reference AG with the IDS filed August 16, 2004). The Raghavan et al. reference provides further support for the asserted utility by providing additional discussion on the importance of the conserved domains of Fc receptors, by discussing the involvement of Fc receptors in immune defense, and by providing evidence that the science related to Fc receptors was wellknown at the time of earliest filing of the present application.

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Applicants assert that the disclosure of both the conserved Fc receptor domains of the FcR-V polypeptide and the reference by Raghaven *et al.* further support the credibility of the asserted specific, substantial, and well-established utility for the FcR-V polypeptide and the corresponding antibodies of the present invention. More specifically, when presented with the evidence indicating that: 1) Fc receptor involvement in immune defense was well-known; 2) Fc receptors contain hallmark Ig-like conserved domains; and 3) the FcR-V polypeptide of the present application contains all hallmark Ig-like domains of Fc receptors, one of skill in the art would expect that the FcR-V polypeptides, and thus antibodies that bind FcR-V, would be useful in treating and/or diagnosing disorders of the immune system, such as, for example, allergy and inflammation.

Despite the evidence presented by Applicants in response to the first office action and summarized herein above, the Examiner responded by issuing a final utility rejection that is *nearly verbatim* to the utility rejection presented in the first office action. *Compare* Paper No. 92004, page 3, last paragraph to page 5, second full paragraph *and* Paper No. 42005, page 3, first full paragraph to page 5, second full paragraph. Applicants respectfully submit that the response provided by the Examiner is improper. As stated in the M.P.E.P.:

Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, <u>unless countervailing evidence can be provided</u> that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement.

Therefore,

[i]f the applicant responds to the *prima facie* rejection, the Office personnel should review the original disclosure, any evidence relied upon in establishing the prima *facie* showing, any claim amendments, and any new reasoning or evidence provided by the applicant in support of an asserted specific and substantial credible utility. It is essential for Office personnel to recognize, fully consider and respond to each substantive element of any response to a rejection based on lack of utility.

See M.P.E.P. § 2107(II)(D) (emphasis added).

## Moreover, the Examiner's response:

must establish that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial. The prima facie showing must contain the following elements: (i) An explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is not both specific and substantial nor well-established; (ii) Support for factual findings relied upon in reaching this conclusion; and (iii) An evaluation of all relevant evidence of record, including utilities taught in the closest prior art.

## See Id. at § 2107(II)(C)(1)(i-iii) (emphasis added).

Given that the presently pending Final Office Action is nearly a verbatim copy of the previous action, it is readily apparent that the Examiner has not responded to "each substantive element" provided in Applicant's rebuttal argument as required by the M.P.E.P.. This is most particularly apparent as it relates to the significance of the conserved domains for FcR-V or the cited Raghaven *et al.* reference, both of which are disclosed in the specification. Most importantly, the Examiner has not provided any explanation, support, or evidence regarding why one of skill in the art would not believe the asserted utility disclosed in the specification when: 1) presented with the knowledge that the FcR-V polypeptide contains all hallmark conserved domains of Fc receptors; 2) given the well-established roles and biological functions of Fc receptors discussed in Raghavan; and 3) provided with information showing that the Fc receptor art was well-known at the time of the earliest filing of the present application.

In addition to the evidence and explanations previously provided, Applicants herein also point out that the specification teaches that FcR-V polypeptides are expressed by activated monocytes, primary dendritic cells, and macrophages. *See, e.g.*, page 13, paragraph 0024. Hence, given the homology of FcR-V to immune system regulatory molecules<sup>2</sup> with the described tissue expression exclusively in cells of the immune system, one of ordinary

<sup>&</sup>lt;sup>2</sup> FcR-V contains three pairs of the Ig-like domains in its extracellular domain located around the three pairs of cysteine residues located at positions 33 and 81, 139 and 179, and 228 and 279 of SEQ ID NO:10. The Fc- $\gamma$ 2 receptor is thought to be important in modulation of the immune and hematopoietic systems. The homology

skill in the art would immediately appreciate that the presently claimed antibodies would be useful in regulating immune system functions.

To corroborate the asserted utility for the FcR-V polypeptide, Applicants previously submitted the post-filing date publication by Tedla *et al.* Applicants provided a sequence alignment showing that the LIR7 polypeptide sequence and the FcR-V polypeptide were identical at amino acid positions –16 to 449. Furthermore, Applicants pointed out that both the LIR7 and FcR-V amino acid sequences have Ig-like domains characteristic of FcRs in addition to short cytoplasmic domains and positively charged arginine residues within their transmembrane domains that are characteristic of activating LIRs. Finally, Applicants disclosed that LIR7 activates immunological and/or inflammatory responses which are well-known to play important roles in host responses to inflammation, allergic diseases and parasitic infections. From this information, Applicants explained that Tedla *et al.* further corroborates the asserted utility that FcR-V polypeptides, and thus, that one of ordinary skill in the art would expect antibodies that bind FcR-V to be useful in treating and/or diagnosing disorders of the immune system, such as allergy and inflammation.

Nonetheless, the Examiner alleges that "the sequence of LIR-7 has been disclosed by Borges *et al.* not by Tedla *et al.*, and that sequence alignment of the claimed SEQ ID NO:10 does not show 100% identity over the referenced polypeptide." See, Paper No. 42005, page 5 fourth full paragraph. In support of this argument, the Examiner provided the results of a database search from SwissProt\_42 database search showing an alignment of 465 amino acids of the FcR-V polypeptide vs. a 482 amino acid sequence.

Applicants respectfully disagree with the Examiner's conclusion. An analysis of the features section of both the SwissProt\_42 analysis provided by the Examiner and the NCBI protein sequence database search for Accession No. Q8N149 (submitted herewith as Exhibit A) reveals that the protein sequence provided by the Examiner actually contains a splice variant at amino acid region 419 to 436. Thus, removal of the splice variant yields a 466 amino acid sequence which was identified by Applicants as LIR7 and which is identical to FcR-V at positions –16 to 449 (SEQ ID NO:10).

between the Fc- $\gamma$ 2 receptor and FcR-V indicates that FcR-V may also be involved in modulation of the immune and hematopoietic systems. See, e.g., pages 19-20, paragraph 0039.

As further evidence that LIR7 is the 466 amino acid sequence previously aligned with FcR-V, Applicants provide herewith the results of a BLAST of the NCBI refseq\_human\_aa database. The BLAST was performed with the FcR-V polypeptide sequence and the results show 100% alignment over 465 amino acids with the NCBI protein Accession No. NP\_006857.1. See BLAST results for alignment gi | 5803068 provided herewith as Exhibit B. An NCBI protein sequence database search result for Accession No. NP\_006857.1 (submitted herewith as Exhibit C) identifies this 466 amino acid protein as "leukocyte immunogobulin-like receptor 7" (i.e., LIR7) (See "Features" section). Furthermore, the search results also list as Reference 2 (residues 1 to 466) the Tedla et al. reference referred to by Applicants herein above and in the previous office action response to corroborate the asserted utility for the FcR-V polypeptide. Thus, Applicants maintain their assertion that the Tedla et al. reference further corroborates the asserted utility of the present invention.

Furthermore, the Ig-like domains characteristic of the Fc receptors and the short cytoplasmic domains and positively charged arginine residues within the transmembrane domains, which are characteristic of activating LIRs, are identical between FcR-V and LIR7. Given the that these domains were well-known as significant contributors to the FcR protein's biological function and given the well-established involvement of FcR proteins in immune responses, one of skill in the art would more likely than not find the asserted utility of the present invention to be specific, substantial, and credible.

Finally, while the Examiner's concedes that "Tedla et al., further teach that LIR7 may have a possible function in tempering Th2 cell dependent inflammatory response" the Examiner alleges that there "is no recitation of FcR-V polypeptide or possible function of said polypeptide in inflammatory response." *See*, Paper No. 42005, page 5, fourth full paragraph.

Initially, Applicants assert that the FcR-V polypeptides, and thus, antibodies that bind FcR-V, are useful in treating and/or diagnosing disorders of the immune system, such as allergy and inflammation. As pointed out in the response to the first office action, the specification teaches that the FcR-V polypeptides, which are important in the regulation of the immune and hematopoietic systems, are "thought to function as an important trigger of complex immune defense responses including phagocytosis, antibody-dependent cellular

cytotoxicity, and release of inflammatory mediators" and "appear to play a role in an early step in type II hypersensitivity reactions." *See*, specification, page 16, paragraph 0032. Additionally, the specification teaches that the FcR-V polypeptides are useful for the diagnosis and/or treatment of specific immune system-related disorders, including

immune-complex related inflammatory diseases such as rheumatoid arthritis, systemic lupus erythmatosis, autoimmune hemolytic anemia, thromboctyopenia and IgG- or IgE-mediated inflammation, anaphylaxis, allergy ....."

See, e.g., page 60, paragraph 0135. Therefore, the specification clearly provides sufficient utility for the FcR-V polypeptide in immune system disorders.

In view of the evidence presented in the response to the first office action and summarized herein, Applicants assert that the totality of the record shows that the asserted utility is well-established, specific, substantial, and credible and therefore the rejection under 35 U.S.C. §101 should be withdrawn. Furthermore, the above evidence and explanations clearly show that the claimed invention has at least one or more patentable utilities. Therefore, Applicants respectfully submit that the rejection of claims 23-36, 40-53, 57-66, and 70-79 under 35 U.S.C. §101 has been obviated and respectfully request that the rejection of the claims be reconsidered and withdrawn.

## Rejection of claims 23-36, 40-53, 57-66, and 70-79 under 35 U.S.C. § 112, first paragraph

The rejection of claims 23-36, 40-53, 57-66, and 70-79 under 35 U.S.C. § 112, first paragraph, is maintained based on the premise that "since the claimed invention is not supported by either a specific and substantial, asserted utility or a well established utility for the reasons set forth in the rejection under 35 USC § 101 above, one skilled in the art clearly would not know how to use the claimed invention." *See*, Paper No. 42005, page 6, item 8.

Applicants respectfully disagree and traverse.

Applicants respectfully submit that, as explained above, claims 23-36, 40-53, 57-66, and 70-79 are supported by specific, substantial, and/or well-established utilities. Hence, in view of the present application's disclosure and the state of the art as of its earliest filing date, Applicants submit that a person having ordinary skill in the art would certainly know how to use the claimed invention. Accordingly, Applicants respectfully request the rejection of

pending claims 23-36, 40-53, 57-66, and 70-79 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

# Rejection of Claims 57-66 and 70-79 under 35 U.S.C. § 112, first paragraph

The rejection of claims 57-66 and 70-79 under 35 U.S.C. § 112, first paragraph, is maintained for allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." See, Paper No. 42005, page 6-7, item 9. In particular, it is asserted that:

Applicant mistakenly assumes that the disclosure of "cell expressing FcR-V" is an equivalent of "FcR-V protein expressed on the surface of a cell". The genus of "Cells expressing FcR-V" reads on soluble FcR-V and membrane-bound FcR-V, while subgenus "FcR-V protein expressed on the suface of a cell" reads only on a membrane-bound form of FcR-V.

See Id. at page 7, item 12, third full paragraph.

In response, Applicants have herein amended independent claims 57 and 70 to read "An isolated antibody or fragment thereof that specifically binds a FcR-V protein expressed from a cell...". Support for this amendment can be found, for example, at page 2, paragraph 0006; and, pages 8-11, paragraph 0017. Accordingly, the rejection to claims 57-66 and 70-79 has been obviated. Thus, Applicants respectfully request that the Examiner's rejection of claims 57-66 and 70-79 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

#### Conclusion

Applicants respectfully request that the above-made amendments and remarks be entered and made of record in the file history of the instant application. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425.

Date: 7/21/2005

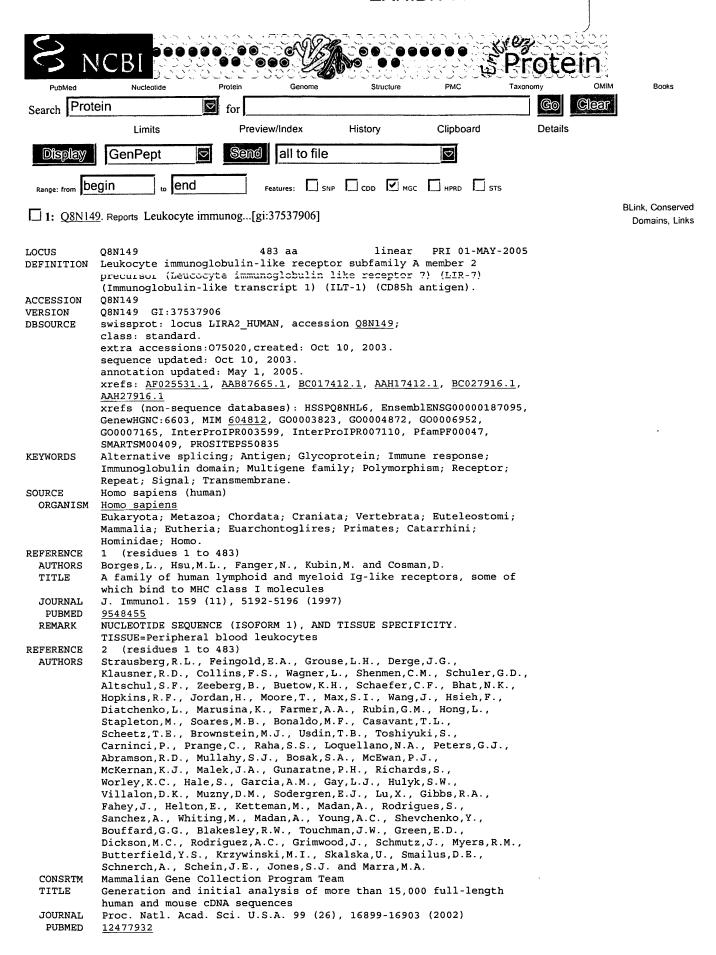
Respectfully submitted,

Doyle A. Siever (1)
Agent for Applicants

(Reg. No. 47,088)

Human Genome Sciences, Inc. 14200 Shady Grove Road Rockville, Maryland 20850 (301) 354-3932 (Phone)

MJP/DAS/PF/ba



```
REMARK
            NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM 2).
            TISSUE=Lung, and Pancreas
            [FUNCTION] May act as receptor for class I MHC antigens.
COMMENT
            [SUBCELLULAR LOCATION] Type I membrane protein.
            [ALTERNATIVE PRODUCTS] Event=Alternative splicing; Named
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            IsoId=Q8N149-2; Sequence=VSP_008455; Note=No experimental
            confirmation available.
            [TISSUE SPECIFICITY] Expression levels are very low or not
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Disclaimer | Write to the Help Desk NCBI | NLM | NIH

Feb 9 2005 14:31:10

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# **EXHIBIT B**

Cmalloat

## **BLAST Results for Result 4416111**

#### **BLAST** results for sequence PF363-FcRV

Accession numbers are hotlinked to Entrez at NCBI The description is hotlinked to the alignment, further down the page

BLASTP 2.0MP-WashU [15-Jun-2000] [sol7-ultra-L64 12:00:28 20-Jun-2000]

Copyright (C) 1996-2000 Washington University, Saint Louis, Missouri USA. All Rights Reserved.

Reference: Gish, W. (1996-2000) http://blast.wustl.edu

Query= PF363-FcRV

(514 letters)

Database: /usr/ncbi/blast/db/refseq\_human\_aa

28,066 sequences; 14,072,078 total letters.
Searching....10....20....30....40....50....60....70....80....90....100% done

				Smallest		
				Sum		
	High	Probabili	ty			
Sequences pr	Score	P(N)	N			
	_					
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gi 5803066	ref		leukocyte immunoglobulin-lik	1734	1.2e-196	2
gi   5031911		NP_005865.1	leukocyte immunoglobulin-lik	1749	1.6e-183	2
gi 5729927		NP_006660.1	leukocyte immunoglobulin-lik	1759	2.2e-182	1
gi 31543056		NP_006856.2	leukocyte immunoglobulin-lik	1756	4.7e-182	1
gi 13324690		NP_077294.1	leukocyte immunoglobulin-lik	1687	9.6e-175	1
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gi 47519953		NP_036408.3	leukocyte immunoglobulin-lik	1474	3.6e-152	1
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gi 13399320			leukocyte immunoglobulin-lik	884	3.1e-101	2
gi 32895361	ref	NP_870994.1	leukocyte Ig-like receptor 9	637	1.8e-63	1
gi 32490553	ref	NP_067073.1	leukocyte Ig-like receptor 9	636	2.3e-63	1
gi   46488946	ref	NP_703144.2	killer cell immunoglobulin-l	579	2.5e-57	1
gi 5803052	ref	NP_006728.1	killer cell immunoglobulin-l	555	8.7e-55	1
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gi 21314641	ref	NP 006838.2	leukocyte immunoglobulin-lik	543	1.6e-53	1
gi 32895363	ref	NP_871714.1	leukocyte Ig-like receptor 9	543	1.6e-53	1
gi 7019441	ref	NP_037421.1	killer cell immunoglobulin-l	538	5.5e-53	1
gi 45505167	ref	NP 001546.2	immunoglobulin superfamily,	545	1.8e-52	1
gi 37574620	ref	NP 057447.3	glycoprotein VI (platelet);	437	2.8e-42	1
gi 41208929	ref	XP_372748.1	similar to 1060P11.3 (killer	433	7.3e-42	1
gi 41151816	ref	XP 373336.1	similar to 1060P11.3 (killer	430	1.5e-41	1
gi 7705568	ref	NP_056952.1	killer cell immunoglobulin-l	423	8.4e-41	1
gi 6912472	ref	NP_036444.1	killer cell immunoglobulin-l	417	3.6e-40	1
gi 7657273	ref	NP_055034.1	killer cell immunoglobulin-l	409	2.6e-39	1
gi 7657271	ref	NP 055033.1	killer cell immunoglobulin-l	401	1.8e-38	1
gi 4758692	ref	NP 004820.1	natural cytotoxicity trigger	340	2.0e-37	2
gi   7657277	ref	NP 055327.1	killer cell immunoglobulin-l	385	8.9e-37	1
gi 11968154	ref	NP 065396.1	killer cell immunoglobulin-l	382	1.9e-36	1
gi   7657279	ref	NP 055328.1	killer cell immunoglobulin-l	369	3.8e-36	2
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gi 31982878	ref	NP 002246.3	killer cell immunoglobulin-l	363	1.9e-34	1
gi   19743857	ref	NP 579803.1	Fc alpha receptor isoform b	274	3.2e-33	2
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gi   19743861	ref	NP 579806.1	Fc alpha receptor isoform d;	310	2.2e-28	1
gi 19743869	ref		Fc alpha receptor isoform h;	227	5.5e-28	2
		NP 579814.1	Fc alpha receptor isoform j;	298	4.9e-27	1
gi 46397359	manufacture and the	NP 036446.2	killer cell immunoglobulin-1	286	1.0e-25	1
qi   46397357		NP 839942.2	killer cell immunoglobulin-l	286	1.0e-25	1
gi 45580719	ref		osteoclast-associated recept	271	4.7e-24	1
		NP 579811.1	Fc alpha receptor isoform q;	264	2.8e-23	1
<u></u>				_01		-

```
    gi | 45580717 | ref | NP | 996553.1 | osteoclast-associated recept...
    234 | 5.3e-20 | 1

    gi | 21071030 | ref | NP | 570602.2 | alpha | 1B-qlycoprotein [Homo ... | gi | 33589850 | ref | NP | 055326.2 | killer cell immunoglobulin-l... | 214 | 7.9e-18 | 1

    gi | 19743865 | ref | NP | 579808.1 | Fc alpha receptor isoform f;... | gi | 10947103 | ref | NP | 067154.1 | leukocyte-associated | Ig-like... | 209 | 2.8e-17 | 1
```

#### HSP Alignment Overview

ID					Seq Length
	1			514	ł
gi 5803068				<del>&gt;</del>	466
gi 5803066	-	<del></del> >		<del>&gt;&gt;</del>	489
gi 5031911			>	<del></del> >	598
gi 5729927				<del></del> >	650
gi 31543056		>>		<del></del> >	439
gi 13324690				<del></del> >	464
gi 5803060				<del></del> >	631
gi 47519953				<del></del> >	499
gi 5803070				<del></del> >	590
- ,	1			514	1

WARNING: Descriptions of 92 database sequences were not reported due to the limiting value of parameter V = 50.

Score = 2489 (881.2 bits), Expect = 9.9e-260, P = 9.9e-260 Identities = 465/465 (100%), Positives = 465/465 (100%)

Query: 1 MTPILTVLICLGLSLGPRTHVQAGHLPKPTLWAEPGSVIIQGSPVTLRCQGSLQAEEYHL 60
MTPILTVLICLGLSLGPRTHVQAGHLPKPTLWAEPGSVIIQGSPVTLRCQGSLQAEEYHL
Sbjct: 1 MTPILTVLICLGLSLGPRTHVQAGHLPKPTLWAEPGSVIIQGSPVTLRCQGSLQAEEYHL 60

Query: 61 YRENKSASWVRRIQEPGKNGQFPIPSITWEHAGRYHCQYYSHNHSSEYSDPLELVVTGAY 120
YRENKSASWVRRIQEPGKNGQFPIPSITWEHAGRYHCQYYSHNHSSEYSDPLELVVTGAY
Sbjct: 61 YRENKSASWVRRIQEPGKNGQFPIPSITWEHAGRYHCQYYSHNHSSEYSDPLELVVTGAY 120

Query: 121 SKPTLSALPSPVVTLGGNVTLQCVSQVAFDGFILCKEGEDEHPQRLNSHSHARGWSWAIF 180
SKPTLSALPSPVVTLGGNVTLQCVSQVAFDGFILCKEGEDEHPQRLNSHSHARGWSWAIF
Sbjct: 121 SKPTLSALPSPVVTLGGNVTLQCVSQVAFDGFILCKEGEDEHPQRLNSHSHARGWSWAIF 180

Query: 181 SVGPVSPSRRWSYRCYAYDSNSPYVWSLPSDLLELLVPGVSKKPSLSVQPGPMVAPGESL 240 SVGPVSPSRRWSYRCYAYDSNSPYVWSLPSDLLELLVPGVSKKPSLSVQPGPMVAPGESL

Sbjct: 181 SVGPVSPSRRWSYRCYAYDSNSPYVWSLPSDLLELLVPGVSKKPSLSVQPGPMVAPGESL 240

Query: 241 TLQCVSDVGYDRFVLYKEGERDFLQRPGWQPQAGLSQANFTLGPVSPSHGGQYRCYSAHN 300 TLQCVSDVGYDRFVLYKEGERDFLQRPGWQPQAGLSQANFTLGPVSPSHGGQYRCYSAHN

Sbjct: 241 TLQCVSDVGYDRFVLYKEGERDFLQRPGWQPQAGLSQANFTLGPVSPSHGGQYRCYSAHN 300

Query: 301 LSSEWSAPSDPLDILITGQFYDRPSLSVQPVPTVAPGKNVTLLCQSRGQFHTFLLTKEGA 360 LSSEWSAPSDPLDILITGQFYDRPSLSVQPVPTVAPGKNVTLLCQSRGQFHTFLLTKEGA

Sbjct: 301 LSSEWSAPSDPLDILITGQFYDRPSLSVQPVPTVAPGKNVTLLCQSRGQFHTFLLTKEGA 360

Query: 361 GHPPLHLRSEHQAQQNQAEFRMGPVTSAHVGTYRCYSSLSSNPYLLSLPSDPLELVVSAS 420 GHPPLHLRSEHQAQQNQAEFRMGPVTSAHVGTYRCYSSLSSNPYLLSLPSDPLELVVSAS

Sbjct: 361 GHPPLHLRSEHQAQQNQAEFRMGPVTSAHVGTYRCYSSLSSNPYLLSLPSDPLELVVSAS 420

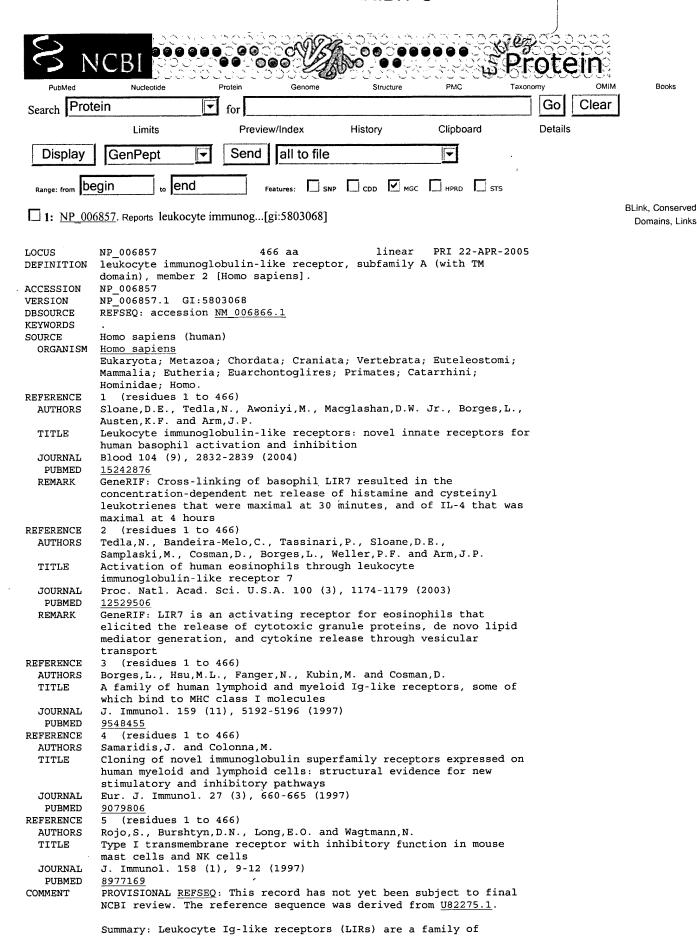
Query: 421 LGQHPQDYTVENLIRMGVAGLVLVVLGILLFEAQHSQRSLQDAAG 465 LGQHPQDYTVENLIRMGVAGLVLVVLGILLFEAQHSQRSLQDAAG

Sbjct: 421 LGOHPQDYTVENLIRMGVAGLVLVVLGILLFEAQHSQRSLQDAAG 465

Score = 1734 (615.5 bits), Expect = 1.2e-196, Sum P(2) = 1.2e-196 Identities = 340/422 (80%), Positives = 355/422 (84%)

```
1 MTPILTVLICLGLSLGPRTHVQAGHLPKPTLWAEPGSVIIQGSPVTLRCQGSLQAEEYHL 60
Query:
            MTPI+TVLICL LSLGPRTHVQAG LPKPTLWAEPGSVI QGSPVTL CQG L+ +EY L
          1 MTPIVTVLICLRLSLGPRTHVQAGTLPKPTLWAEPGSVITQGSPVTLWCQGILETQEYRL 60
Sbjct:
         61 YRENKSASWVRRI-QEPGKNGQFPIPSITWEHAGRYHCQYYSHNHS-SEYSDPLELVVTG 118
Ouery:
            YRE K+A W+ RI QE K GQFPIPSITWEH GRY C Y SH
                                                         SE SDPLELVVTG
Sbjct:
         61 YREKKTAPWITRIPQEIVKKGQFPIPSITWEHTGRYRCFYGSHTAGWSEPSDPLELVVTG 120
Query:
        119 AYSKPTLSALPSPVVTLGGNVTLQCVSQVAFDGFILCKEGEDEHPQRLNSHSHARGWSWA 178
            AY KPTLSALPSPVVT GGNVTL CVSQVAF FILCKEGEDEHPQ LNS
        121 AYIKPTLSALPSPVVTSGGNVTLHCVSQVAFGSFILCKEGEDEHPQCLNSQPRTHGWSRA 180
Sbict:
        179 IFSVGPVSPSRRWSYRCYAYDSNSPYVWSLPSDLLELLVPGVSKKPSLSVQPGPMVAPGE 238
Query:
            IFSVGPVSPSRRWSYRCYAYDSNSP+VWSLPSDLLELLV GVSKKPSLSVQPGP+VAPGE
        181 IFSVGPVSPSRRWSYRCYAYDSNSPHVWSLPSDLLELLVLGVSKKPSLSVQPGPIVAPGE 240
Sbjct:
        239 SLTLQCVSDVGYDRFVLYKEGERDFLQRPGWQPQAGLSQANFTLGPVSPSHGGQYRCYSA 298
Query:
            SLTLQCVSDV YDRFVLYKEGERDFLQ PG QPQAGLSQANFTLGPVS S+GGQYRC A
        241 SLTLQCVSDVSYDRFVLYKEGERDFLQLPGPQPQAGLSQANFTLGPVSRSYGGQYRCSGA 300
Sbict:
Query:
        299 HNLSSEWSAPSDPLDILITGGFYDRPSLSVQDVDTVAPGKNVTLLCQSRGQFHTFLLTKE 258
            +NLSSEWSAPSDPLDILI GOF RP +SV P PTVA G+NVTLLCQS G FHTFLLTK
Sbjct:
        301 YNLSSEWSAPSDPLDILIAGQFRGRPFISVHPGPTVASGENVTLLCQSWGPFHTFLLTKA 360
        359 GAGHPPLHLRSEHQAQQNQAEFRMGPVTSAHVGTYRCYSSLSSNPYLLSLPSDPLELVVS 418
Query:
                PL LRS H+ + QAEF M PVTSAH GTYRCY SLSSNPYLLS PSD LEL+VS
        361 GAADAPLRLRSIHEYPKYQAEFPMSPVTSAHSGTYRCYGSLSSNPYLLSHPSDSLELMVS 420
Sbjct:
        419 AS 420
Query:
Sbjct:
        421 GA 422
Score = 477 (173.0 bits), Expect = 6.7e-64, Sum P(2) = 6.7e-64
Identities = 126/321 (39%), Positives = 177/321 (55%)
        111 PLELVVTGAYSKPTLSALPSPVVTLGGNVTLQCVSQVAFDGFILCKEGEDEHP--QRLNS 168
Ouerv:
            P V G KPTL A P V+T G VTL C + + L +E + P R+
         17 PRTHVQAGTLPKPTLWAEPGSVITQGSPVTLWCQGILETQEYRLYREKKTA-PWITRIPQ 75
Sbict:
        169 HSHARGWSWAIFSVGPVSPSRRWSYRCYAYDSNSPYVWSLPSDLLELLVPGVSKKPSLSV 228
Query:
                                YRC+ Y S++ WS PSD LEL+V G KP+LS
                +G
                     F + ++
Sbjct:
         76 EIVKKGO----FPIPSITWEHTGRYRCF-YGSHTAG-WSEPSDPLELVVTGAYIKPTLSA 129
        229 QPGPMVAPGESLTLQCVSDVGYDRFVLYKEGERDFLQRPGWQPQA-GLSQANFTLGPVSP 287
Query:
             P P+V G ++TL CVS V + F+L KEGE + Q
                                                    QP+ G S+A F++GPVSP
        130 LPSPVVTSGGNVTLHCVSQVAFGSFILCKEGEDEHPQCLNSQPRTHGWSRAIFSVGPVSP 189
Sbjct:
Query:
        288 SHGGQYRCYSAHNLSSE-WSAPSDPLDILITGQFYDRPSLSVQPVPTVAPGKNVTLLCQS 346
                YRCY+ + S WS PSD L++L+ G
                                              +PSLSVQP P VAPG+++TL C S
        190 SRRWSYRCYAYDSNSPHVWSLPSDLLELLVLG-VSKKPSLSVQPGPIVAPGESLTLQCVS 248
Sbjct:
        347 RGQFHTFLLTKEGAGHPPLHLRS-EHQAQQNQAEFRMGPVTSAHVGTYRCYSSLS-SNPY 404
Query:
               + F+L KEG L L + QA +QA F +GPV+ ++ G YRC + + S+ +
        249 DVSYDRFVLYKEGE-RDFLQLPGPQPQAGLSQANFTLGPVSRSYGGQYRCSGAYNLSSEW 307
Sbjct:
        405 LLSLPSDPLELVVSASLGQHP 425
Query:
              S PSDPL+++++
Sbjct:
        308 -- SAPSDPLDILIAGQFRGRP 326
Score = 285 (105.4 bits), Expect = 1.4e-38, Sum P(2) = 1.4e-38
Identities = 71/207 (34%), Positives = 112/207 (54%)
         28 KPTLWAEPGSVIIQGSPVTLRCQGSLQAEEYHLYRENKSASWVRRIQEPGKNGQ----- 81
Query:
           KP+L +PG ++ G +TL+C + + + LY+E +
                                                       +Q PG
Sbjct:
        225 KPSLSVQPGPIVAPGESLTLQCVSDVSYDRFVLYKEGERDF----LQLPGPQPQAGLSQA 280
         82 -FPIPSITWEHAGRYHCQYYSHNHSSEYS---DPLELVVTGAY-SKPTLSALPSPVVTLG 136
Query:
             F + ++ + G+Y C ++N SSE+S DPL++++ G + +P +S P P V G
Sbjct:
        281 NFTLGPVSRSYGGQYRCSG-AYNLSSEWSAPSDPLDILIAGQFRGRPFISVHPGPTVASG 339
Query:
        137 GNVTLQCVSQVAFDGFILCKEGEDEHPQRLNS-HSHARGWSWAIFSVGPVSPSRRWSYRC 195
             NVTL C S F F+L K G + P RL S H + +
                                                    A F + PV+ +
        340 ENVTLLCQSWGPFHTFLLTKAGAADAPLRLRSIHEYPK--YQAEFPMSPVTSAHSGTYRC 397
Sbjct:
        196 YAYDSNSPYVWSLPSDLLELLVPGVSK 222
Query:
```

```
S++PY+ S PSD LEL+V G ++
Sbict:
        398 YGSLSSNPYLLSHPSDSLELMVSGAAE 424
Score = 182 (69.1 bits), Expect = 1.2e-196, Sum P(2) = 1.2e-196
Identities = 36/37 (97%), Positives = 37/37 (100%)
        424 HPQDYTVENLIRMGVAGLVLVVLGILLFEAQHSQRSL 460
            HPQDYTVENLIRMG+AGLVLVVLGILLFEAQHSQRSL
        453 HPQDYTVENLIRMGIAGLVLVVLGILLFEAQHSQRSL 489
Sbjct:
>gi|5031911 ref|NP_005865.1| leukocyte immunoglobulin-like receptor, subfamily
           B (with TM and ITIM domains), member 2; leukocyte
           immunoglobulin-like receptor 2 [Homo sapiens]
           Length = 598
Score = 1749 (620.7 bits), Expect = 1.6e-183, Sum P(2) = 1.6e-183
Identities = 340/427 (79%), Positives = 361/427 (84%)
          1 MTPILTVLICLGLSLGPRTHVQAGHLPKPTLWAEPGSVIIQGSPVTLRCQGSLQAEEYHL 60
Query:
            MTPI+TVLICLGLSLGPRTHVQ G +PKPTLWAEP SVI QGSPVTL COGSL+A+EY L
          1 MTPIVTVLICLGLSLGPRTHVQTGTIPKPTLWAEPDSVITQGSPVTLSCQGSLEAQEYRL 60
Sbjct:
         61 YRENKSASWVRRIQ-EPGKNGQFPIPSITWEHAGRYHCQYYSHNHSSEYSDPLELVVTGA 119
Query:
            YRE KSASW+ RI+ E KNGQF IPSITWEH GRY CQYYS
                                                        SE SDPL LV+TGA
         61 YREKKSASWITRIRPELVKNGQFHIPSITWEHTGRYGCQYYSRARWSELSDPLVLVMTGA 120
Sbjct:
Query:
        120 YSKPTLSALPSPVVTLGGNVTLQCVSQVAFDGFILCKEGEDEHPQRLNSHSHARGWSWAI 179
            Y KPTLSA PSPVVT GG VTLQC SQVAF GFILCKEGEDEHPQ LNS HARG S AI
        121 YPKPTLSAQPSPVVTSGGRVTLQCESQVAFGGFILCKEGEDEHPQCLNSQPHARGSSRAI 180
Sbjct:
        180 FSVGPVSPSRRWSYRCYAYDSNSPYVWSLPSDLLELLVPGVSKKPSLSVQPGPMVAPGES 239
Query:
            FSVGPVSP+RRWS+RCY YD NSPYVWS PSDLLELLVPGVSKKPSLSVQPGP+VAPGES
        181 FSVGPVSPNRRWSHRCYGYDLNSPYVWSSPSDLLELLVPGVSKKPSLSVQPGPVVAPGES 240
Sbict:
        240 LTLOCVSDVGYDRFVLYKEGERDFLQRPGWQPQAGLSQANFTLGPVSPSHGGQYRCYSAH 299
Query:
            LTLQCVSDVGYDRFVLYKEGERD Q PG QPQAGLSQANFTLGPVS S+GGQYRCY A+
        241 LTLQCVSDVGYDRFVLYKEGERDLRQLPGRQPQAGLSQANFTLGPVSRSYGGQYRCYGAY 300
Sbjct:
        300 NLSSEWSAPSDPLDILITGQFYDRPSLSVQPVPTVAPGKNVTLLCQSRGQFHTFLLTKEG 359
Query:
            NLSSEWSAPSDPLDILITGQ + P +SVQP PTVA G+NVTLLCQS QFHTFLLTK G
Sbjct:
        301 NLSSEWSAPSDPLDILITGQIHGTPFISVQPGPTVASGENVTLLCQSWRQFHTFLLTKAG 360
        360 AGHPPLHLRSEHQAQQNQAEFRMGPVTSAHVGTYRCYSSLSSNPYLLSLPSDPLELVVSA 419
Query:
               PL LRS H+ + QAEF M PVTSAH GTYRCY SL+S+PYLLS PS+PLELVVS
        361 AADAPLRLRSIHEYPKYQAEFPMSPVTSAHAGTYRCYGSLNSDPYLLSHPSEPLELVVSG 420
Sbjct:
Query:
        420 -SLGQHP 425
             S+G P
Sbjct:
        421 PSMGSSP 427
Score = 479 (173.7 bits), Expect = 1.7e-49, Sum P(2) = 1.7e-49
Identities = 125/328 (38%), Positives = 172/328 (52%)
         17 PRTHVQAGHLPKPTLWAEPGSVIIQGSPVTLRCQGSLQAEEYHLYRENKSASWVRRIQEP 76
Query:
               V G PKPTL A+P V+ G VTL+C+ + + L +E +
        112 PLVLVMTGAYPKPTLSAQPSPVVTSGGRVTLQCESQVAFGGFILCKEGEDEHPQCLNSQP 171
Sbjct:
         77 GKNGO----FPIPSITWEHAGRYHCQYYSHNHSSEYSDP---LELVVTGAYSKPTLSALP 129
Query:
               G F + ++ + C Y N +S P LEL+V G KP+LS P
        172 HARGSSRAIFSVGPVSPNRRWSHRCYGYDLNSPYVWSSPSDLLELLVPGVSKKPSLSVQP 231
Sbjct:
        130 SPVVTLGGNVTLQCVSQVAFDGFILCKEGEDEHPQRLNSHSHARGWSWAIFSVGPVSPSR 189
Query:
             PVV G ++TLQCVS V +D F+L KEGE + Q L G S A F++GPVS S
Sbjct:
        232 GPVVAPGESLTLQCVSDVGYDRFVLYKEGERDLRQ-LPGRQPQAGLSQANFTLGPVSRSY 290
        190 RWSYRCY-AYDSNSPYVWSLPSDLLELLVPG-VSKKPSLSVQPGPMVAPGESLTLQCVSD 247
Query:
               YRCY AY+ +S WS PSD L++L+ G + P +SVQPGP VA GE++TL C S
Sbjct:
        291 GGQYRCYGAYNLSSE--WSAPSDPLDILITGQIHGTPFISVQPGPTVASGENVTLLCQSW 348
        248 VGYDRFVLYKEGERDFLQRPGWQPQAGLSQANFTLGPVSPSHGGQYRCYSAHNLSSEW-- 305
Query:
                                         QA F + PV+ +H G YRCY + N S
              + F+LKG D R
        349 ROFHTFLLTKAGAADAPLRLRSIHEYPKYQAEFPMSPVTSAHAGTYRCYGSLN-SDPYLL 407
Sbjct:
        306 SAPSDPLDILITGQFYDRPSLSVQPVPT 333
Ouerv:
```



```
cells. All LIRs in subfamily B have an inhibitory function (see,
           e.g., LILRB1, MIM 604811). LIRs in subfamily A, with short
           cytoplasmic domains lacking an immunoreceptor tyrosine-based
           inhibitory motif (ITIM) and with transmembrane regions containing a
           charged arginine residue, may initiate stimulatory cascades. One
           member of subfamily A (LILRA3; MIM 604818) lacks a transmembrane
           region and is presumed to be a soluble receptor. [supplied by OMIM].
FEATURES
                     Location/Qualifiers
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /chromosome="19"
                     /map="19q13.4"
                     1..466
     Protein
                     /product="leukocyte immunoglobulin-like receptor,
                     subfamily A (with TM domain), member 2"
                     /note="leukocyte immunoglobulin-like receptor 7"
     CDS
                     1..466
                     /qene="LILRA2"
                     /coded_by="NM_006866.1:88..1488"
                     /note="go component: integral to membrane [goid 0016021]
                     [evidence IEA];
                     go_function: antigen binding [goid 0003823] [evidence TAS]
                     [pmid 9548455];
                     go_function: receptor activity [goid 0004872] [evidence
                     TAS] [pmid 9548455];
                     go_process: immune response [goid 0006955] [evidence IEA];
                     go process: signal transduction [goid 0007165] [evidence
                     TAS] [pmid 9548455]"
                     /db_xref="CCDS:CCDS12900.1"
                     /db xref="GeneID: 11027"
                     /db xref="MIM:604812"
ORIGIN
        1 mtpiltvlic lglslgprth vqaghlpkpt lwaepgsvii qgspvtlrcq gslqaeeyhl
       61 yrenksaswv rriqepgkng qfpipsitwe hagryhcqyy shnhsseysd plelvvtgay
      121 skptlsalps pvvtlggnvt lqcvsqvafd gfilckeged ehpqrlnshs hargwswaif
      181 svgpvspsrr wsyrcyayds nspyvwslps dllellvpgv skkpslsvqp gpmvapgesl
      241 tlqcvsdvgy drfvlykege rdflqrpgwq pqaglsqanf tlgpvspshg gqyrcysahn
      301 lssewsapsd pldilitgqf ydrpslsvqp vptvapgknv tllcqsrgqf htflltkega
      361 ghpplhlrse hqaqqqaef rmgpvtsahv gtyrcyssls snpyllslps dplelvvsas
421 lgqhpqdytv enlirmgvag lvlvvlgill feaqhsqrsl qdaagr
//
```

immunoreceptors expressed predominantly on monocytes and B cells and at lower levels on dendritic cells and natural killer (NK)

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Feb 9 2005 14:31:10